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Patent and Trademark Office

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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
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09/242,561 02/19/99 SATO

Y 10235/4

023838 HM12/0202  
KENYON & KENYON  
1500 K STREET, N.W., SUITE 700  
WASHINGTON DC 20005

EXAMINER

FORMAN, R

ART UNIT

PAPER NUMBER

1655

DATE MAILED:

02/02/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

# Office Action Summary

Application No.

09/242,561

Applicant(s)

SATO, YOSHIHIRO

Examiner

BJ Forman

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

## Status

- 1) ☒ Responsive to communication(s) filed on 22 January 2001.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

## Disposition of Claims

- 4) ☒ Claim(s) 21,22,25,26,32-34 and 36-39 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☐ Claim(s) 21,22,25,26,32-34 and 36-39 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claims \_\_\_\_\_ are subject to restriction and/or election requirement.

## Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are objected to by the Examiner.
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved.
- 12) ☐ The oath or declaration is objected to by the Examiner.

## Priority under 35 U.S.C. § 119

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

## Attachment(s)

- 15) ☒ Notice of References Cited (PTO-892)
- 16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 17) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) \_\_\_\_\_
- 18) ☒ Interview Summary (PTO-413) Paper No(s). 12
- 19) ☐ Notice of Informal Patent Application (PTO-152)
- 20) ☐ Other:

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# DETAILED ACTION

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Response to papers filed 16 January 2000 in Paper No. 11 in which claims 34 & 36 were amended and claims 23,24,27,28,30, 31 & 35 were amended have been thoroughly reviewed and entered. The previous amendments in the Office Action of Paper No. 9 dated 30 October 2000 under 35 U.S.C. 112, second paragraph are withdrawn in view of the previous rejections under 35 U.S.C. 103(a) are withdrawn in view of the

The finality of the previous office action is withdrawn in view of the new grounds for rejection. New grounds for rejection are discussed. Currently claims 21, 22, 25, 26, 29, 32-34, 36-39 are under prosecution.

## Claim Rejections - 35 USC § 112

### First paragraph of 35 U.S.C. 112: Written Description

Following is a quotation of the first paragraph of 35 U.S.C. 112: The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention. Claims 34-39 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

protection  
descriptive  
Description  
determining whether the invention has been set forth by other descriptions of the invention in possession of the claimed invention.  
35 U.S.C. § 112, p 1 "Written Description"  
January 5, 2001; II Methodology for Reducing

The claims are drawn to a process for protecting from evaporation. The claim encompasses each comprising a myriad of reagents, reagent preparations, reactions, reaction parameters and environmental and chemical conditions wherein each reaction requires specific and exact reagents, reagent preparations, reagent conditions, environmental conditions and chemical conditions to obtain the desired results. However, the specification does not describe an actual reduction to practice of the invention as claimed. The specification teaches a process for conducting one reaction i.e. PCR (page 3, last paragraph and pages 23-56) and the specification teaches that the invention is "effective for a biochemical reactions other than PCR which involves a high temperature reaction" (page 8, bottom paragraph). While the specification teaches the actual reduction to practice of a PCR reaction, the specification does not teach reduction to practice one other reaction of the very large genus of reactions claimed. Therefore, the specification does not teach an actual reduction to practice of the invention as claimed.

as  
rejections under  
466. No. 4, Friday,  
Written Description (3.1).

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The claims are drawn to a process for conducting a reaction in a minute droplet protected from evaporation however, the specification does not provide an adequate written description of the claimed invention. The methodology for determining adequacy of Written Description to convey that applicant was in possession of the claimed invention includes determining whether the application describes an actual reduction to practice, determining whether the invention is complete as evidenced by drawings or determining whether the invention has been set forth in terms of distinguishing identifying characteristics as evidenced by other descriptions of the invention that are sufficiently detailed to show that applicant was in possession of the claimed invention (*Guidelines for Examination of Patent Applications under 35 U.S.C. § 112, p 1 "Written Description" Requirement*; Federal Register/ Vol 66. No. 4, Friday, January 5, 2001; II Methodology for Determining Adequacy of Written Description (3.)).

Reduction to practice

The claims are drawn to a process for conducting a reaction in a minute droplet protected from evaporation. The claimed reaction encompasses a very large genus of reactions, each comprising a myriad of reagents, reagent preparations, reactions, reaction parameters and environmental and chemical conditions wherein each reaction requires specific and exact reagents, reagent preparations, reagent conditions, environmental conditions and chemical conditions to obtain the desired results. However, the specification does not describe an actual reduction to practice of the invention as claimed. The specification teaches a process for conducting one reaction i.e. PCR (page 3, last paragraph and pages 23-56) and the specification teaches that the invention is "effective for a biochemical reactions other than PCR which involves a high temperature reaction" (page 8, bottom paragraph). While the specification teaches the actual reduction to practice of a PCR reaction, the specification does not teach reduction to practice one other reaction of the very large genus of reactions claimed. Therefore, the specification does not teach an actual reduction to practice of the invention as claimed.

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Completed by drawings

The claims are drawn to a process for conducting a reaction in a minute droplet protected from evaporation. The specification teaches a process for conducting PCR as evidenced by drawing. However, the specification does not teach that the invention as claimed is complete as evidenced by drawings because the specification does not teach any other of the very large genus of reactions claimed as evidenced by drawings. The drawings of the specification illustrate the process of reducing evaporation (Fig. 1-42) but the drawings do not provide evidence that the invention is complete because the drawings do not provide or complete the description of the process for conducting a reaction in a minute droplet protected from evaporation. Therefore, the drawing do not provide a teaching of the process as claimed.

Description of identifying characteristics

The claims are drawn to a process for conducting a reaction in a minute droplet protected from evaporation. The claimed reaction encompasses a very large genus of reactions, each comprising a myriad of reagents, reagent preparations, reactions reaction parameters and environmental and chemical conditions wherein each reaction requires specific and exact reagents, reagent preparations, reagent conditions, environmental conditions and chemical conditions to obtain the desired results. The specification teaches a process for conducting a reaction i.e. PCR (page 3, last paragraph and pages 23-56) and the specification teaches that the invention is "effective for a biochemical reaction other than PCR which involves a high temperature reaction" (page 8, bottom paragraph). The specification does not teach identifying characteristics of the claimed reactions e.g. reagents, conditions, and preparations. Therefore, the specification has not been set forth in terms of distinguishing identifying characteristics as evidenced by other descriptions of the invention.

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The courts have stated that the specification must describe the claimed invention in sufficient detail that one skilled in the art can reasonably conclude the inventor had possession of the claimed invention see *In re Vas-Cath, Inc.* 935F2d. 1555, 1563, 19 USPQ2d 1111,1116.

The specification does not provide a written description of the claimed invention in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. Therefore, the specification does not provide an adequate written description of the claimed invention.

### **Response to Arguments**

4. Applicant argues that one skilled in the art would not have to undertake undue experimentation to achieve the desired results i.e. reduced evaporation because the oily liquid layers provide the desired results. The arguments are deemed moot in view of the withdrawn rejection under 35 U.S.C. 112, first paragraph: Scope of Enablement. However, the arguments are discussed as it pertains to the new grounds for rejection under 35 U.S.C. 112, first paragraph: Written Description.

The arguments are not found persuasive because the method of Claims 34-39 is drawn to a process for conducting a reaction in a minute droplet and therefore the "desired result" is conducting a reaction. The specification teaches conducting a PCR reaction. As stated above, the claimed reaction encompasses a myriad of reactions comprising a myriad of reagents, reagent preparations, reaction conditions, environmental conditions and chemical conditions wherein each reaction requires specific and exact reagents, reagent preparations, reagent conditions, environmental conditions and chemical conditions to obtain the desired reaction. However, the specification does not teach the myriad of claimed reactions and therefore, the specification does not provide a written description of the invention as claimed.

Applicant further argues that the specification teaches methods for testing whether a particular oily layer would reduce evaporation on pages 20-21 and therefore the specification satisfies the requirements of 35 U.S.C. 112, first paragraph. This argument is not found persuasive because as stated above, the method of Claims 34-39 is drawn to a process for conducting a reaction in a minute droplet which encompasses a myriad of reactions. The specification teaches one reaction i.e. PCR and therefore, the specification does not provide a written description of the invention as claimed.

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**35 U.S.C. 112, second paragraph: Indefinite**

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 21-39 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a. Claims 21-32 are indefinite in Claim 21 for the recitation "providing a minute aqueous droplet" because "aqueous" lacks proper antecedent basis in the preamble of the claim. It is suggested that Claim 21 be amended to provide proper antecedent basis e.g. in Claim 21, line 1 insert "aqueous" before "droplet".

b. Claim 33 is indefinite in the recitation "providing a minute aqueous droplet" because "aqueous" lacks proper antecedent basis in the preamble of the claim. It is suggested that the claim be amended to provide proper antecedent basis e.g. in line one insert "aqueous" before "droplet".

c. Claims 34-39 are indefinite in Claim 34 for the recitation "providing a minute aqueous droplet" because "aqueous" lacks proper antecedent basis in the preamble of the claim. It is suggested that Claim 34 be amended to provide proper antecedent basis e.g. in Claim 34, line 1 insert "aqueous" before "droplet".

***Claim Rejections - 35 USC § 102***

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

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8. Claims 21, 22, 25, 26, 29, 34 & 36 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Monk et al. (Mammalian development: a practical approach, 1987) in view of the teaching of Drohan et al. al. (U.S. Patent No. 5,589,604, issued 31 December 1996)

Regarding Claim 21, Monk et al. discloses a process comprising the steps of: providing a planar substrate (cover slip); providing an oily liquid layer (liquid paraffin); and providing a minute aqueous droplet (egg) to contact said substrate, said minute droplet being immiscible with said liquid layer, wherein said oily liquid layer surrounds all surfaces of said minute aqueous droplet that are not in contact with said substrate whereby evaporation is reduced i.e. (ii) drops of Sendai virus solution and PNC medium are place on the cover slip, (iii) the chamber is filled with liquid paraffin, and (iv) the eggs are introduced into the liquid paraffin (page 244, Nuclear Transfer). Monk et al. do not specifically teach that the process reduces evaporation of the minute droplet. However, Drohan et al. teach the process of Monk et al. reduces evaporation of the minute droplet (Column 9, lines 34-36). Therefore, the process disclosed by Monk et al. reduces evaporation of the minute droplet.

Regarding Claim 22, Monk et al. disclose the process wherein said planar substrate is water repellent i.e. the substrate is a cover slip which is glass and therefore water repellent (page 244, 3.1 (i)).

Regarding Claim 25, Monk et al. disclose the process wherein said oily liquid layer is paraffin oil (page 244 (iii)).

Regarding Claim 26, Monk et al. disclose the process wherein said droplet (egg) is shot into said oily liquid layer i.e. the eggs are introduced into the liquid paraffin (page 244, (iv)).

Regarding Claim 29, Monk et al. disclose the process further comprising providing a covering over said liquid layer i.e. the bottom of the chamber comprises the covering over the liquid layer (page 245, Fig 4b).

Regarding Claim 34, Monk et al. Discloses a process for conducting a reaction in a minute droplet protected from evaporation comprising the steps of: providing a planar



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substrate (cover slip); providing an oily liquid layer (liquid paraffin); and providing a minute aqueous droplet (eggs to be manipulated) to contact said substrate; said minute droplet being immiscible with said liquid layer, providing a covering (bottom of the chamber) in contact with said oily liquid layer, wherein said oily liquid layer surrounds all surfaces of said minute aqueous droplet that are not in contact with said contact surface of said planar substrate; providing to said protected minute droplet a reactant (donor DNA); and conducting a reaction in said minute droplet with said reactant whereby evaporation is reduced i.e. (ii) drops of Sendai virus solution and PNC medium are place on the cover slip, (iii) the chamber is filled with liquid paraffin, and (iv) the eggs are introduced into the liquid paraffin (Nuclear Transfer: 3.1 page 244), a donor pronucleus is injected and a fusion reaction is conducted (3.3 pages 246-248 and Fig 5a-h).

Regarding Claim 36, Monk et al. discloses the process wherein said aqueous minute droplet comprises DNA i.e. donor pronucleus (page 247, Fig. 5).

### ***Claim Rejections - 35 USC § 103***

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

10. Claims 21-33, 38 & 39 are rejected under 35 U.S.C. 103(a) as being unpatentable over Monk et al. (Mammalian development: a practical approach, 1987), Brown et al. (U.S. Patent No. 5,807,522 filed 7 June 1995) and Sambrook et al. (Molecular Cloning: A laboratory Manual, 2<sup>nd</sup>, 1992).

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Regarding Claims 21-32, Monk et al. teaches the process for reducing evaporation of a minute droplet comprising the steps of: providing a planar substrate (cover slip); providing an oily liquid layer (liquid paraffin); and providing a minute aqueous droplet (eggs to be manipulated) to contact said substrate; said minute droplet being immiscible with said liquid layer, wherein said oily liquid layer surrounds all surfaces of said minute aqueous droplet that are not in contact with said substrate whereby evaporation is reduced i.e. (ii) drops of Sendai virus solution and PNC medium are place on the cover slip, (iii) the chamber is filled with liquid paraffin, and (iv) the eggs are introduced into the drops surround by the liquid paraffin (page 244, Nuclear Transfer), wherein said planar substrate is water repellent (page 244, 3.1 (i)), wherein said oily liquid layer is paraffin oil (page 244 (iii)), wherein said droplet (egg) is shot into said oily liquid layer i.e. the eggs are introduced into the liquid paraffin (page 244, (iv)), and further comprising providing a covering over said liquid layer i.e. the bottom of the chamber comprises the covering over the liquid layer (page 245, Fig 4b) and wherein an aqueous solution is adjacent to the aqueous droplet i.e. the egg is surrounded by the PNC medium (page 244, (ii)-(iv)) but they do not teach the aqueous solution does not contact said droplet. However, It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify adjacent solution of Monk et al. with additional solution adjacent, but not in contact with the aqueous droplet for the expected benefit of maintaining the positioning and environment of the egg during manipulation.

Regarding Claim 33, Monk et al. teaches the process for reducing evaporation of a minute droplet comprising the steps of: providing a planar substrate (cover slip); providing an oily liquid layer (liquid paraffin); and providing a minute aqueous droplet (eggs to be manipulated) to contact said substrate; said minute droplet being immiscible with said liquid layer, wherein said oily liquid layer surrounds all surfaces of said minute aqueous droplet that are not in contact with said substrate whereby evaporation is reduced i.e. (ii) drops of Sendai virus solution and PNC medium are place on the cover slip, (iii) the chamber is filled with liquid

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paraffin, and (iv) the eggs are introduced into the liquid paraffin (page 244, Nuclear Transfer), and further comprising providing a covering over said liquid layer i.e. the bottom of the chamber comprises the covering over the liquid layer (page 245, Fig 4b) but Monk et al. does not teach said covering in contact with said minute aqueous droplet. However, it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify cover taught by Monk et al. with a cover in contact with the minute droplet because the skilled practitioner in the art would have been motivated to place the cover in contact with the microdroplet for the expected benefit of reducing the optical distortion resulting from light passing from the aqueous droplet through the oily liquid to thereby reduce optical distortion during micro-manipulations and to more accurately manipulate and detect the manipulation.

Regarding Claim 37, Monk et al. do not teach the process wherein the contact surface between said substrate and said minute droplet comprises an enzyme adsorption preventing agent. However, one skilled in the art would have known that reactions involving nucleic acids utilize enzyme adsorption preventing agents e.g. SDS. Specifically, Sambrook et al. teach that Denhardt's reagent which contains SDS is used in nucleic acid assays to block non-specific binding reactions (page 9.48). Therefore, It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to apply the teaching of Sambrook et al. to the reaction performed in a minute droplet based on reaction being performed for the expected benefit of reducing non-specific binding as taught by Sambrook et al.

Regarding Claim 38, Monk et al. teaches the process wherein following the reaction, the manipulated micro droplets (eggs) are shot into (transferred into) the oily liquid layer wherein the contact between said substrate and said minute droplet comprises bovine serum albumin (page 244, last line) but they do not teach the initial substrate comprises bovine serum albumin. However, it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the planar substrate taught by Monk et al. by adding the bovine serum albumin for the expected benefit of eliminating the step of transferring the

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droplet from one substrate to a second substrate for the added benefit of reduced risk of injuring or disrupting the droplet (egg).

Regarding Claim 39, Monk et al. teaches the process wherein the oily liquid is paraffin oil (page 244 (iii)) but they do not teach the thickness of the oily liquid. However, oily liquids of 100 $\mu$ m thickness were known and routinely practiced in the art at the time the claimed invention was made and it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the oily layer taught by Monk et al. with a oily layer of 100 $\mu$ m or less using routinely practiced procedures to obtain the claimed invention because the skilled practitioner in the art would have been motivated to provide very thin oily layer having 100 $\mu$ m or less thickness for the obvious benefit of reducing optical distortion during micro-manipulations to thereby more accurately manipulate and detect the manipulation.

#### **Prior Art of Record**

11. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure: Drohan et al. (U.S. Patent No. 5,589,604, issued 31 December 1996) teach a process for preventing evaporation and for conducting a reaction in a minute droplet comprising: providing a planar substrate, an oily liquid layer and a minute aqueous droplet to contact said substrate (Column 9, lines 22-47). Kosak et al. (U.S. Patent No. 5,413,924, issued 9 May 1995) teach a method for preventing evaporation in a minute droplet comprising: providing a substrate, an oily layer and a minute aqueous droplet (Abstract). Krivohlavek et al. (U.S. Patent No. 5,505,877, issued 9 April 1996) teach a process for preventing evaporation in droplet comprising: providing a substrate; an oily liquid layer; and an aqueous droplet (Abstract).

#### **Conclusion**

12. No claim is allowed.

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13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to BJ Forman whose telephone number is (703) 306-5878. The examiner can normally be reached on 6:45 TO 4:15.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones can be reached on (703) 308-1152. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 308-8724 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

BJ Forman, Ph.D.  
February 2, 2001

*S. E. Forman*  
S. E. Forman  
February 2, 2001